REFERENCES

1. Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. The sixth report of the Joint National Committee on the Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC VI). Arch Intern Med 1997; 157:2413-46.
2. Estacio RO, Jeffers BW, Hiatt WR, Biggerstaff SL, Gifford N, Schrier RW. The effect of nisoldipine as compared with enalapril on cardiovascular outcomes in patients with non-insulin-dependent diabetes and hypertension. N Engl J Med 1998; 338:645-52.

Salmeterol for Nocturnal Asthma

Lockey RF, DuBuske LM, Friedman B, Petrocella V, Cox F, Rickard K. Nocturnal asthma: effect of salmeterol on quality of life and clinical outcomes. Chest 1999; 115:666-73.

Clinical question **Does salmeterol (Serevent) improve quality of life and clinical outcomes in patients who have moderate asthma with nocturnal symptoms?**

Background Patients who have asthma with nocturnal symptoms have poor sleep quality and decreased daytime cognitive function compared with healthy patients. Many recent clinical trials evaluating specific treatment interventions have included tools assessing quality-of-life parameters in addition to measuring objective outcomes. This trial was designed to study the effect of the long-acting β-agonist salmeterol on quality-of-life and clinical outcomes of patients with asthma.

Population studied A total of 474 patients with asthma were recruited from US specialty clinics. All subjects had a forced expiratory volume in 1 second (FEV_1) of 40% to 80% of predicted norms, documented semireversible airway obstruction, nocturnal symptoms, and a decrease in waking peak expiratory flow (PEF). All of the subjects used inhaled albuterol as needed. In addition, 112 regularly took theophylline, and 301 regularly used inhaled corticosteroids. Patients were excluded if they were pregnant or lactating, were ill, used another long-acting β-agonist, were on controller medications other than theophylline or inhaled corticosteroids, or had recent controller medication dosage changes. The mean age was 39 years (range = 12 to 76 years).

Study design and validity This was a randomized double-blinded placebo-controlled multicenter clinical trial. Subjects were randomly assigned to receive either inhaled salmeterol 42 µg twice daily or inhaled placebo twice daily while continuing their prestudy medications. They were instructed to keep diaries documenting albuterol use and frequency of nighttime asthma-related awakenings. They were also asked to rate their asthma symptoms. Baseline asthma quality-of-life questionnaire, FEV_1, and PEF data were collected. Subjects were evaluated at 4, 8, and 12 weeks using questionnaire scores, pulmonary function tests, and diary review. Those experiencing an exacerbation during the study were treated at the discretion of the investigators. Data were analyzed on an intention-to-treat basis.

Outcomes measured Outcomes measured included questionnaire scores, FEV_1, PEF, nighttime awakenings, asthma symptoms, and supplemental albuterol use.

Results The treatment groups were similar at baseline. Both treatment groups showed significant improvement in their asthma quality-of-life scores compared with baseline ($P \leq .001$). However, improvement in the salmeterol group was significantly greater than in the placebo group ($P \leq .005$). The PEF measurements of the salmeterol group were significantly improved compared with placebo at all intervals ($P \leq .002$). At 8 and 12 weeks, FEV_1 measurements in the salmeterol group were significantly improved compared with placebo ($P \leq .004$). By week 12, the salmeterol group had 49% less asthma-related awakenings from baseline compared with a 21% decrease in these events in the placebo group ($P < .001$; number needed to treat [NNT] = 3.6). Also by week 12, salmeterol had significantly reduced mean daytime symptom scores by 50% from baseline; the placebo group had a 26% reduction in these scores ($P < .001$). The number of subjects experiencing an asthma exacerbation was significantly higher in the placebo group than with the salmeterol group (30% vs 20%, respectively; $P = .02$; NNT = 10). Rates of study withdrawal due to adverse events were similar: 6% in the placebo group and 4% in the salmeterol group. Insomnia (2%) and headache (2%) were reported separately by patients in the salmeterol group compared with 0% for each in the placebo group. This difference did not reach statistical significance.

Recommendations for clinical practice **Adding salmeterol to the treatment regimen of clinically stable adolescents and adults with moderate asthma experiencing nocturnal symptoms significantly improves self-reported asthma-related quality-of-life scores and clinical outcomes. These results support the National Institutes of Health's current asthma guidelines. The guidelines encourage physicians to add long-acting bronchodilators to the treatment regimen of patients with moderate asthma who are already taking anti-inflammatory medication and continue to have daytime or nighttime symptoms.[1] Clinicians should anticipate future studies comparing long-acting inhaled β-agonists in**

patients with nocturnal asthma symptoms to determine which agents are most efficacious, cost-effective, and have the fewest adverse effects.

Sean Bryan, MD
Thomas Jefferson University
Philadelphia, Pennsylvania
E-mail: Sbryan0310@aol.com

REFERENCE

1. National Asthma Education and Prevention Program. Highlights of the expert panel report 2: guidelines for the diagnosis and management of asthma. Bethesda, Md: National Institutes of Health; 1997. Publication no. 97-4051A.

An Alternative Treatment for Low Back Pain

Ghoname EA, Craig WF, White PF, et al. Percutaneous electrical nerve stimulation for low back pain: a randomized crossover study. JAMA 1999; 281:818-23.

Clinical question **Does percutaneous electrical nerve stimulation (PENS) improve pain and functioning in patients with chronic low back pain?**

Background Low back pain is one of the most common and disabling problems in our society, and current therapies are mostly unsatisfactory. Newer research has shown that PENS is effective for management of pain associated with low back pain. This study compares PENS with transcutaneous electrical nerve stimulation (TENS) and exercise therapy in the treatment of low back pain caused by degenerative disc disease.

Population studied Sixty patients participated in the study. Participants had chronic (>3 months) stable low back pain, were taking oral nonopiod analgesics, had radiologically confirmed degenerative disc disease, and had no acute or long-term illnesses. Patients with drug or alcohol abuse, long-term opioid use, a change in the character or severity of the pain within the last 3 months, presence of sciatica, previous use of nontraditional analgesic therapies, pending medicolegal litigation, or inability to complete a health status assessment questionnaire were excluded from the study. The population seems similar to that of the typical family practice, but demographic information (eg, diagnostic work-up, duration of pain, back operations, disability, or referral pattern) is lacking, and would have provided additional clues to understanding which patients could most benefit from this therapy.

Study design and validity This randomized sham-controlled crossover study compared sham-PENS, PENS, TENS, and flexion-extension exercise during a 15-week study period. The PENS therapy consisted of 10 32-gauge acupuncture-like needle probes placed to a 2- to 4-cm depth in a dermatomal distribution of the pain; electrical stimulation was then applied with intensity adjusted to produce a tapping sensation without muscle contractions. The sham-PENS therapy was identical, except that electrical stimulation was not applied. Each patient received one of the 4 treatment modalities for 30 minutes 3 times a week for 3 weeks, according to 1 of 4 computer-generated sequences.

The study design is strong. Its strengths include randomization of modality sequence, the crossover design, blinded collection of data, inclusion of the sham-PENS control group and a wash-out period, and clinically relevant outcomes. The lack of emphasis on confounding variables (eg, disability status), and the small numbers (limiting the power for detecting confounders) are the main weaknesses.

Outcomes measured Pain response, physical activity, quality of sleep, and sense of well-being were measured using visual analog scales (VASs) and the physical and mental component scores of the 36-Item Short-Form Health Survey (SF-36). Oral analgesic requirements and adverse effects were recorded in daily diaries. An overall assessment of relative effectiveness was obtained at the completion of all modalities. Useful outcomes that were not measured include cost (both financial and time) and feasibility of obtaining each service (clinical setting and capable providers).

Results All patients completed the study. PENS produced a significant improvement from baseline in mean VAS scores for pain and level of activity (P <.03), and from sham-PENS, TENS, or exercise (P <.02). The SF-36 scores corroborated these findings. PENS also decreased consumption of nonopioid analgesics from 2.6 pills (±1.4) per day to 1.3 pills (±1.2) per day (P <.008), while the other 3 modalities did not. PENS was the preferred therapy for 91% of the study patients, and greater than 80% of patients indicated they would be willing to pay extra to receive PENS therapy. The authors did not comment on the patients' reported adverse effects.

Recommendations for clinical practice **This study provides fairly strong evidence that PENS therapy is superior to TENS, exercise, and placebo in providing short-term pain relief and improved physical function for patients with chronic low back pain. When confronted with the frustrations of the limited options for low back pain, physicians should consider PENS as a potential alternative. Future research is needed on the utility for acute low back pain, cost-effectiveness, use in combination with other modalities, ideal**